

THE
AMERICAN JOURNAL
OF THE MEDICAL SCIENCES

FEBRUARY, 1919

ORIGINAL ARTICLES

CLINICAL STUDIES IN CUTANEOUS ASPECTS OF
TUBERCULOSIS.

I. "TUBERCULOUS" PURPURA, ERYTHEMA MULTIFORME AND
ERYTHEMA NODOSUM.

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THE tendency of recent advances in the study of the etiology of dermatoses has been, increasingly, to show that many supposed clinical entities, so styled on purely morphological grounds, have a multiple etiology. One of the conditions undergoing such etiological revision is the erythema group, including the clinical entities of erythema multiforme and erythema nodosum. The work of revising our outlook on erythema multiforme, purpura and urticaria was well begun by Osler in 1895. Erythema nodosum is of particular interest because on its border lie erythema induratum and the group of dermatoses designated after Darier as "tuberculids," whose intimate relation to tuberculosis is now generally accepted. Erythema nodosum, on the basis of the experimental evidence cited herein, is in a fair way to be at least partially allied to this group, and it awaits only a sufficient body of clinical evidence and some corroborative work to establish its connection. The fact that the majority of American dermatological texts have not yet given this phase of the matter the attention it deserves, probably accounts for the seeming unfamiliarity of internists, surgeons and general diagnosticians, with the very great diagnostic and prognostic significance of purpura, erythema multiforme, erythema nodosum and the tuberculids. My

VOL. 157, NO. 2.—FEBRUARY, 1919.

own interest in the relation of this group of dermatoses to tuberculosis was aroused by the death of a patient having the miliary type of the disease, following an onset in the form of purpura rheumatica and succeeded by erythema multiforme.

The material here presented forms part of a series of approximately forty cases of erythema nodosum, erythema multiforme with purpura, erythema induratum and the various types of papuloneerotic tuberculids seen on the service of the Section on Dermatology of the Mayo Clinic during the past two years (1916-1917). The material is presented in a separate communication in the hope of emphasizing the possibility of this form of onset of tuberculosis and of arousing the attention of diagnosticians and internists in this country to its importance from the standpoint of diagnosis and treatment.

The literature on the subject of the association of erythema nodosum with tuberculosis was ably reviewed in 1914 by Foerster, who reported 2 cases of his own. A large proportion of the cases recorded elsewhere were in children. Since Foerster's summary, articles by Nicola (who also cites De Blasi) and Jaquero have appeared: the former reported 6 and the latter 2 cases. Cecicac considers the good effect of heliotherapy an evidence of the tuberculous origin of the disease. The French investigators, including Chauffard, Sezary, Marfan, Brian and Landouzy, have been especially active in the study of erythema nodosum and have been vigorous proponents of the theory of tuberculous etiology. Landouzy, for example, by his successful inoculation of tuberculosis into guinea-pigs by material from the lesions of erythema nodosum, has supplied the best experimental evidence of the tuberculous nature of certain forms of the disease. Brian has accomplished a similar result. Hildebrandt, in 1907, reported inoculation from the blood at the height of the attack, but interprets his results with reservations.

One of the very interesting features of the etiological developments concerning erythema nodosum is the demonstration by Rosenow in 1915 of a polymorphous gram-negative diphtheroid as the cause of the condition. This organism, whose infection-atrium is apparently the tonsils and pus pockets about the teeth, gives rise especially to the more acute types of the disease. The pathology of erythema nodosum, however, is such that it seems a rash assumption to attribute the changes to a single type of organism. There would appear to be no reason why embolic infarction or thrombosis of terminal vessels in the skin of the extremities, and varying grades of exudation and inflammatory reaction about the affected vessels, could not be produced by living tubercle bacilli in a hypersensitive individual, as suggested by the studies of Rist and Rolland, or by the dead bodies or the "toxins" of the same organism, as suggested by the experiments of Chauffard. While with a larger experience we may

come to recognize clinical differences between erythema nodosum produced by the tubercle bacillus or its products and that produced by the Rosenow diphtheroid, or perhaps by streptococci, the assumption that the pathological differences between the various types will be striking and pathognomonic is in the present uncertain state of knowledge gratuitous. It seems not unlikely that the clinician who ascribes too high a degree of etiological specificity to a condition such as erythema nodosum will fail to recognize many important relations of the picture and will overlook other etiological possibilities which may be of the greatest import to the particular case.

The 10 cases which form the subject of this report in contrast with a number of those reported in the literature occurred in adults. The youngest patient was sixteen years of age, the oldest forty-three; the majority over twenty-five.

CASE 1 (A-202732), a girl, aged twenty-four years, an indoor worker, gave a negative family and personal history. The patient complained chiefly of a cough and an eruption on the legs. For four weeks she had had a slight sore-throat but no tonsillitis. Two days after the onset of the pharyngitis, erythematous nodes, varying from 2.5 to 5 cm. in diameter and from eight to ten in number, appeared over the pretibial region. In color, tenderness, induration and tenseness the lesions were typically those of erythema nodosum; they improved under salicylates and rest. The patient's temperature subsided in two weeks from onset. She had lost 21 pounds in weight during the four weeks of the attack. She coughed, with some expectoration, but a negative sputum examination; no night-sweats or hemoptysis. Examination of the chest indicated signs of a doubtful character over the right lower lobe, with suggestive but not pathognomonic findings in the roentgenogram. The diagnosis was regarded as indeterminate, and the patient was placed at once on antituberculous hygiene. She improved, recovered weight and remained well, although she did not work for six months. In February she had grippe, which lasted more than two months, with loss of strength, weight and appetite. The patient was reexamined in June, nearly a year after the attack of erythema nodosum. At this time breath sounds were prolonged over the right lobe and the whispered sounds were markedly increased. No evidence of active tuberculosis could be recognized in the roentgenogram. She had no temperature, hemoptysis, increased pulse, nervousness or sweats. Antituberculous hygiene was continued, with the patient under observation.

This case from a dermatological point of view was a classical erythema nodosum in every morphological detail. No focus of infection in the form of bad tonsils or infected or abscessed teeth was apparent. The question as to whether or not the patient is tuberculous is, of course, *sub judice*, but should be viewed in the light of the following case.

CASE 2 (A-49238), a male, aged thirty-eight years, has been under observation in the Clinic for seven years. In 1911 he was referred for treatment by his home physician because of shifting pains, stiffness and purpura of ten days' duration. While the patient's physician conceded that the purpura suggested rheumatism, he personally was inclined to suspect tuberculosis of which, in miliary form, the patient's sister had died. Six months before the onset of symptoms the patient had been in bed with "typhoid" for twelve days. At the time of examination purpuric lesions were present on the shins, shoulders and chest. A rise in temperature was reported; he had lost appetite but no weight. Evanescent rales were heard posteriorly over the left lung. Enlarged glands in the left axilla and cervical regions were noted and the roentgenogram showed beginning tuberculosis of both apices; the sputum, however, was negative. In 1914 the patient was again seen for a brief period, but the tuberculous process was then quiescent. In 1918, seven years after the onset of the purpura and three years after the patient was last observed, my assistant was called to see him during an attack of erythema nodosum, which I had the opportunity to observe as it was subsiding. At this time numerous deep subcutaneous erythematous nodes over the tibiae and many less erythematous, smaller and paler shotty indurations, were found. The chain of lymphatics along the left pectoralis major and the axillary and mammary nodes were enlarged and, in some instances, caseous and calcified. Subsequent resection of these glands at operation established the pathological diagnosis of tuberculosis.

This case differed from the conventional picture of erythema nodosum only in the greater pallor and smaller size of many of the nodules, in the absence of the ecchymotic color changes and in the generally lesser activity of the process. At its height, however, it was quite within the usual limits of variation of the clinical picture of erythema nodosum. The purpura, with rheumatoid pains in the early years of the disease observed in this patient, is one of the features common to other cases to be cited hereinafter.

The following case is illustrative of the manner in which a purpuric onset and a tubercleulid may precede, by months or years, the gross clinical evidence of active tuberculosis.

CASE 3 (A-154673), a man, aged thirty-one years, a tailor, first came to the Clinic in 1916 because of a serotal hernia, which was operated on, with good results. At that time the patient gave a history the significance of which was not appreciated until later. A year before his first examination he had an attack of grippe followed by a purpuric eruption. The macules were from a pinhead to a dime in size; some of them had "blistered" and left scars on the extremities. Apart from a small colloid goitre, a hernia and a liehenified scrotum his examination was negative. No radiographic examination was considered necessary in view of the absence of

symptoms. One year and a half after this examination and the operation for hernia the patient returned, giving a history of "sciatica," and of an abscess that had drained through the buttock, and had left a persistent sinus. Bismuth injection demonstrated a draining sacro-iliac abscess. The patient was then seen by a dermatological consultant because of the scars on the legs, which were typically those of a tubercle, although there were then no active lesions. The operation on the sinus disclosed a tuberculous process, probably originating in the lumbar or sacral spine.

If a dermatologist had seen the purpura and the tubercle at the first examination two years previously and appreciated its significance a more thorough search might have disclosed the focus.

CASE 4 (A-157847), a woman, aged thirty-three years, a clerical worker, came to the Clinic, in 1916, with a history of severe anemia two years before, from which she had recovered under treatment with iron. A year later a lump, not, however, preceded by any sore-throat; appeared on the right side of the neck. In fact, the patient had never had sore-throat or tonsillitis. Abruptly, two months after coming to the Clinic, and nearly two years after the appearance of the glands, the legs swelled markedly without apparent cause and were covered with raised, red lumps. The patient had a temperature of 103° and was confined to bed for two weeks; the temperature subsided but the edema persisted. Examination disclosed a pale, rather fat girl, with numerous erythematous nodules and hyperemic plaques on both legs and arms. The plaques in particular were more suggestive of erythema multiforme than of the conventional erythema nodosum. Their comparative pallor may have been due to the anemia. None of the lesions had shown any tendency to ulceration. The temperature was normal; hemoglobin, 40 per cent.; a marked glandular enlargement on the right side of the neck was shown, by subsequent excision for diagnosis, to be tuberculous. The radiograph of the chest showed healed pulmonary tuberculosis, involving both apices. The tonsils were markedly septic. After the removal of the tuberculous glands a tonsillectomy was performed. This, however, did not prevent the continued appearance of nodular lesions on the legs. Although these did not at any time become ulcerative, the picture approached more and more nearly that of erythema induratum of Bazin, for which we treated the patient a year later.

The typical onset of erythema nodosum in this case, two years after the appearance of the glands, was combined with the appearance of lesions suggestive of erythema multiforme. The nodose lesions persisted and recurred, constituting a chronic erythema nodosum, so to speak, even after tonsillectomy had removed a possible atrium of infection for diphtheroid and other organisms and a block dissection had removed a portion of the tuberculous

focus. There was nothing to suggest a dental source of infection. That the tuberculous focus which was the probable source and perpetuator of the process had not been done away with, is shown by the subsequent re-operation for recurrences in the glands. The following is a case of somewhat similar type:

CASE 5 (A-22802), a girl, aged twenty-three years, a rancher, three years before coming to the Clinic, had sustained surgical removal of cervical glands and tonsillectomy, at which time a pathological diagnosis of tuberculous adenitis was made. The tuberculous process had extended to new glands in spite of tuberculin and an outdoor regime. For two weeks before her examination in the Clinic she had felt tired and her legs had ached, following which an eruption of "lumps" appeared abruptly below the knees on the posterior surface of the legs. These were beginning to involute spontaneously. On examination bluish moderately infiltrated plaques were recognized on the calves of the legs; these disappeared under appropriate treatment. The roentgenogram of the chest was negative. The tuberculous nature of the adenitis had been established by the previous pathological examination and there was a visible and palpable recurrence.

The onset in this case suggests a mild erythema nodosum. In its distribution on the calves and in the relative indolence of the lesions it approached more nearly the type of erythema induratum and should be compared with the preceding case and the last case in the series. The whole picture developed three years after the removal of a tonsillar focus, but while the tuberculous focus was still active. The next case, while perforce left indeterminate, illustrates very well the type of erythema nodosum onset which may eventuate in an active tuberculosis such as that suspected in Case 1 and identified in Case 2.

CASE 6 (A-188556), a man, aged forty-four years, reported at the Clinic with the statement that three weeks before he had caught a common cold. He felt weak since the onset of the infection and had had a cough and expectoration for two weeks. There were some aching and edema of the legs. The past respiratory history was not significant. On examination a very marked right cervical adenopathy was found. The patient's afternoon temperature was 100°. The extensor surfaces of the arms and legs were studded with deep-seated nodules varying from 0.5 to 1.5 cm. in diameter and from a yellowish pink to a deep violaceous color. Over the anterior tibial region there were numerous larger lesions, which were, on the whole, however, somewhat smaller and less ecchymotic than those of a well-developed erythema nodosum, and showed signs of early involution. The lesions about the wrists were of the erythema multiforme type and few in number. A few papulopustules had appeared. Examination of the thorax disclosed prolonged breath sounds and increased fremitus over the right apex. The radio-

graphic examination of the chest, a Wassermann test and the blood culture were all negative.

This case is especially instructive because, in addition to presumptive signs of tuberculosis in the form of localized lymphadenitis, the cutaneous manifestations included erythema multiforme lesions about the wrists, erythema nodosum over the tibiae and a few pustular lesions suggesting the acute generalized military tuberculosis of the skin seen in children and more rarely in adults. The lung signs were inconclusive but suggestive.

The next case illustrates how the appearance of an erythema multiforme as a manifestation of obscure tuberculosis may be followed by the development of a tubercle. The history aligns itself with that of Case 3 (A-154673), who gave a history of a purpura followed by a papulonecrotic tubercle, as an illustration of the importance of the individual history of cutaneous manifestations in a proper interpretation of the relation of purpura and erythema multiforme to tuberculosis.

CASE 7 (A-224920), a young girl, aged sixteen years, gave an extraordinary family history, on the mother's side, of tuberculosis in both direct and collateral lines. The mother herself had been examined in the Clinic, although not by a dermatologist, and the presence of "yellowish-brown stain-like spots" on the legs had been noted. A diagnosis of anemia and septic teeth was made in the mother's case; the daughter was referred to us on a provisional diagnosis of Raynaud's disease because of the cyanosis of her hands and the history of attacks of "blisters" on the fingers. Her father described to us a fairly typical though abortive attack of erythema multiforme, involving the hands and wrists, which had preceded the present trouble by about four years. The description of the condition at the time of the examination was that of a vernal attack of folliculitis, of which the scars were distinctly visible on the dorsal aspects of the terminal phalanges. Similar lesions had developed on the toes. The general examination disclosed the presence of rales and increased dullness over the right lung apex, although the examiner was not in the least under the influence of a preconceived notion about the case, since he had made a diagnosis of Raynaud's disease. Although the roentgenogram of the chest was negative, we advised, in view of the history and the tubercle scars, that an antituberculous regimen be adopted. The tonsils had been removed for recurrent tonsillitis four years before the onset of the folliculitis.

The last case of the series illustrates the association of purpura with a typical tubercle, erythema induratum and the prominence of arthritic symptoms, which might well lead to misinterpretation of the process in its earlier stages as a septic or rheumatic infection.

CASE 8 (A-233765), a very large, florid woman, aged thirty years, decidedly overweight, whose father had died of empyema and lung

trouble, was referred to my service for a very typical erythema induratum with papuloneerotic lesions and ulceration involving the calves of both legs. On examination it was found that the patient had many cutaneous nodes scattered over both extremities, with purpuric lesions over the arms, trunk and chest. She had an arthralgia and myalgia of the right shoulder which prevented her from raising her arm to her head, and reported that six years before she had had "rheumatic fever." The tuberculid antedated the "rheumatism" by eight years. The teeth were negative, tonsils only slightly septic, roentgenogram of the chest negative and no glands were identified. The tuberculid responded rapidly to treatment, but the nodules in the upper extremities continued to recur.

This case represents a type of patient not unfamiliar to both dermatologist and internist in which a florid and rather obese exterior conceals a focus of tuberculosis which at times cannot be identified. The case is included with the series to illustrate the association of purpura, with a cutaneous lesion whose tuberculous character is now generally conceded.

Before summarizing the lessons to be drawn from such a series of cases I shall further illustrate the diagnostic problems presented by erythema nodosum from the standpoint of tuberculosis by two examples drawn from clinically typical erythema nodosum, diagnosed as such in my records, but with the reservation that observation of their cases shall be continued for some time.

CASE 9 (A-194220), a woman, aged thirty-two years, indoor worker, after being "under the weather" for some time, presented herself looking decidedly ill. She complained of a slight sore-throat, arthritis of the knees and ankles and of having numerous large, deep infiltrated nodose lesions of a dark reddish to purplish color in the pretibial region and on the front of the thighs. Typical lesions of erythema multiforme were found on the backs of the hands and on the neck. There was nothing in the history to lead one to suspect tuberculosis. The tonsils were markedly septic and several alveolar abscesses were demonstrated by the radiogram. The patient showed, however, physical signs of a slight right-sided pleurisy at the base, and the radiogram was suspicious. The erythema nodosum disappeared entirely on salicylates, after which the pyogenic foci were removed and she improved rapidly, all pulmonary signs disappearing to such an extent that a contemplated sanitarium regime was given up.

There are no signs of a tuberculous process in this case four months after the attack of erythema nodosum, but an experience with erythema nodosum of the type illustrated by the foregoing cases would lead one to insist on further observation. Petroff, it will be recalled, has directed attention to the effect of intercurrent infection in temporarily lighting up tuberculous foci to the point at which they can be recognized for a brief time, only to disappear again with the sub-

sidence of the incidental infection. Abt, in 1907, also suggested that it was the function of erythema nodosum to prepare the way for tuberculosis, a conception which loses none of its plausibility in this type of case by the further belief that there may be a true tuberculous erythema nodosum represented by the first eight cases of this series as well.

CASE 10 (A-235299), a housewife, aged twenty-seven years, presented the lesions of erythema nodosum over the front of the thighs and pretibial region, many of them large and tumid, with marked arthritic onset. The patient had lost 15 pounds in weight during eight weeks of the acute process before she was first seen. She exhibited a definite hyperpigmentation overlying a pasty pallor. A history of tonsillitis some years before was obtained. The lesions were not and had not been painful, although in all other particulars they conformed to the strict erythema nodosum type, even to the ecchymotic changes. The tonsils were not septic and the radiogram of the teeth was negative. The patient had a unilateral phlyctenular conjunctivitis, not especially suggestive of tuberculosis. On the other hand, the radiogram of the thorax showed a markedly thickened right hilus, indicating enlarged glands.

Although the patient made an almost miraculous recovery under salicylates it would be folly to release her from further observation for the settlement of the question of concealed tuberculosis. Had her symptoms been accepted at their face value no investigation of this question would have been made and the condition would have been regarded as "rheumatic."

DISCUSSION AND SUMMARY. The series here presented is too small for a satisfactory statistical summary, and for that reason will be incorporated for interpretation in another paper with the group of tuberculids of which it forms a part. Briefly, however, it is of interest to note that the clinical picture of tuberculous purpura, tuberculous erythema multiforme and tuberculous erythema nodosum is made up of objective rather than subjective symptoms. Estimated by a rigorous standard, 4 of the first 8 cases were positively demonstrated as tuberculous, and the remaining 4 were of a highly suspicious nature if not absolutely definite; 2 additional cases of erythema nodosum, morphologically conforming to the conventional or rheumatic type, were also suspected of being tuberculosis and are under observation. Of the 8 original cases the tuberculous focus in 4 was identified by pathological examination; 2 were positive and 1 indeterminate in the roentgenogram of the chest; 4 showed physical signs in the lung and 1 was indeterminate, and 4 had visible and palpable adenopathy. No evidence of syphilis could be identified in any of the 10 cases; 2 of the patients had tuberculids of the papulonecrotic and erythema induratum type, and 1 of them had folliculitis, a tuberculid of the fingers; 3 presented purpuric lesions, 3 had lesions of the erythema multiforme type

and 6 had nodular lesions of the type met with in erythema nodosum, though of varying grades of acuteness and severity. In 2 of the cases of nodular erythema the onset was that of erythema nodosum and the localization approached that of erythema induratum. In 1 of these cases the nodose lesions were associated with a typical erythema induratum with ulceration.

Of the 8 cases in the original group 3 presented a family history of tuberculosis and in 1 it was strongly suspected though not absolutely definite. That the onset of the cutaneous manifestations is not necessarily coincident with the onset of the tuberculous infection is apparent from the fact that the shortest probable duration of the active process varied in the cases reported from five months to eight years. The usual points of inquiry in a history of tuberculosis, as to night-sweats, hemoptysis, etc., yielded little information. Two patients only had cough, none had night-sweats and none showed blood in the sputum. The sputum of the 2 who coughed was negative. On the other hand 5 of the 7 of whom data were available showed increased temperatures during the active process, varying from 99° to 103°. Only 1 presented a significant anemia (40 per cent. hemoglobin). The absence of leukocytosis or the presence of a slight leukopenia even in the febrile cases was notable and in keeping with the suspected tuberculous etiology. The counts varied from 5000 to 9600.

The habits and general condition of the patients afforded little clue to the nature of the disturbance, since the septic cases were indistinguishable from the tuberculous. Loss of weight does not seem to have been a conspicuous feature, although 3 out of the 10 cases discussed showed sharp drops, from 8 to 21 pounds in from five to eight weeks.

The consideration of the possibility of a septic focus in these cases was of interest. In 1 of the patients the tonsils did not seem involved, in 2 they were mildly septic but not markedly affected; a fourth with markedly infected tonsils had them removed without appreciable effect on the process and 2 developed their first attack, 1 of erythema nodosum and the other of folliculitis three and four years after the removal of the tonsils. While gross examination for an alveolar or gingival focus was negative throughout the series of 10 cases, in 1 suspected case the patient had an alveolar abscess demonstrable by the radiogram; 2 cases were negative. Radiograms of the teeth were not taken in the remainder. The secondary focus of pyogenic or diphtheroid infection seems to be a negligible quantity in this group, although its importance is much more apparent in a review of the entire series of tuberculids; 4 in 10 had symptoms of a rheumatic character, in the form of myalgia, arthralgia and neuritis. The modes of onset in the 10 cases were slight sore-throat in 2, cold and grippe in 2, typhoid, so-called, in 1 and by indefinite non-localizing symptoms or the typical abrupt onset of

erythema nodosum in 5. The part played by the respiratory atrium is much more apparent in the larger series.

Dermatologically the differentiation of tuberculous from streptococcal or diphtheroid erythema nodosum can scarcely be worked out on so small a group of cases. A tentative personal view of the matter is as follows: While the two conditions are at times indistinguishable from each other on the score of acuteness, localization and course, and this fact cannot be too forcibly emphasized, the following table embodies the main points of difference as the writer has seen them:

STREPTOCOCCAL ERYTHEMA NODOSUM.

Nodes larger, more edematous, and brawny, more tense, and hemorrhagic. May reach the size of a small palm.

Greater involvement of the superficial tissues.

Distribution more apt to be over the front of the lower extremities, especially below the knees and over the front of the thigh; also around the larger joints.

Color changes, more marked than in the tuberculous type. The brown element especially marked. Behaves typically like a bruise.

Symptoms in general more severe, progress more rapid, whole process more acute, tendency to self-limited course.

TUBERCULOUS ERYTHEMA NODOSUM.

Nodes smaller, less marked peripheral reaction, hemorrhagic changes less marked. In their place may be purplish lividity, but usually only a well-developed erythema.

Nodules more circumscribed and deeper.

May appear on either front or back of the leg, but tends to localize posteriorly. May appear in smaller numbers or in crops or groups, or one or two on the upper extremities. May appear on the feet.

The nodule is paler at the onset, and progresses from pink to a livid purple or bluish tinge. If it persists (as erythema induratum) it remains bluish, softens and may show a bullous surface or undergo necrotic sloughing. The nodules may present only a mild erythema which subsides, leaving no color changes or only a faint yellow stain, or there may be colorless ones among the erythematous nodes, suggesting Wondé's nodular tuberculosis of the hypoderm.

Process more indolent, lesions less tender or even painless, more persistent, may last months or longer, especially if there is little inflammatory reaction. Of material assistance in diagnosis is the concomitant occurrence of an indubitable tubercle, such as follicle, or the papulonecrotic types of lesions or their scars.

Our experience with the diagnostic problems involved in erythema nodosum has led us to formulate for ourselves a series of procedures which should be carried out in all cases in order to establish or eliminate the possibility of a tuberculous infection. First of all, a painstaking search of family and past history for evidence of tuberculosis should be made even though the case seems typically of the rheumatoid type. In the same way the histories of patients suspected of having tuberculosis might well be canvassed for evidences of purpura, erythema multiforme and erythema nodosum. In my experience with the larger group of tuberculids I have been

impressed many times with the fact that a rheumatoid onset in this group of dermatoses should suggest tuberculosis almost as promptly as it does a focus of streptococcal infection. Arthritic and myalgic symptoms seem to have little differential value in eliminating tuberculous infection in these cases. Since the evidences of associated tuberculous infection in this group of conditions are largely objective, painstaking examination of the chest for physical signs, and by roentgenograms should be made in every case. The throat and accessory sinuses should be examined for a collateral focus of pyogenic infection and a radiogram of the teeth should also be a part of the routine examination. Systematic observation of the temperature should be undertaken, with a leukocyte count. A careful search for enlarged glands should be made and repeated. I believe that cases of erythema nodosum are of sufficiently grave prognostic significance to warrant a period of observation and reexamination, prolonged in proportion to the suspicions developed by the study of the case. Finally, I venture to suggest the aid which dermatological consultation can render in such cases. One is surprised to see the readiness with which competent and even highly trained internists dismiss a purpura as "rheumatic," failing entirely to notice the tuberculid, or its scars, which lie beside it, or speculate on the probability of Hodgkin's disease in an adenitis when the evidence to prove it tuberculous is before their eyes in the form of a crop of papulonecrotic lesions. A certain amount of special experience and some special attention to this detail will add much to the diagnostic armamentarium of men in other fields who are called on to diagnose and deal with tuberculosis as a medical and surgical problem.

CONCLUSIONS. 1. While it is impossible at the present time to dogmatize on the existence of a tuberculous type of purpura, erythema multiforme or erythema nodosum, clinical and experimental evidence is collecting to show a close association between a tuberculous infection and cutaneous syndromes of the type mentioned. Whether the lesions themselves are due to the tubercle bacillus, and whether or not their appearance signalizes a flare-up in the tuberculous focus, cannot as yet be definitely stated. It is possible that a non-tuberculous infection which produces the erythema complex may uncover the tuberculous focus, so to speak, much as measles is known to do, and permit a lighting up of a lesion otherwise quiescent. The transition stages apparently existing between erythema nodosum on the one hand and erythema induratum and the tuberculids on the other, together with the experimental evidence cited, would seem to make this view the less probable one. The more probable one, in my opinion, is that which harmonizes with current conceptions of the etiology of tuberculids—that the purpuric, erythematous and nodose lesions are cutaneous reactions to heterogeneously distributed tubercle bacilli, deposited in a hypersensitive

skin and originating in a tuberculous focus sometimes unrecognized perhaps for many years. Whether the tuberculous phase is the cause or the consequence, the frequent clinical association of the cutaneous symptoms with this disease loses none of its importance from the standpoint of diagnosis and therapy.

2. Since the clinical appearance of the eruptions discussed does not in my opinion offer adequate means of differentiating "tuberculous" from non-tuberculous forms, every case of purpura, and many cases of erythema multiforme, should, I believe, be subjected to a preliminary survey for the possibility of tuberculous infection. Every case of erythema nodosum should be subjected to an even more searching examination.

3. The search for a focus of tuberculosis should employ the usual evidence elicited from the history, weight and temperature curves and radiograms and physical examination for pulmonary and glandular signs (present in 8 out of 10 of the cases) here presented. The teeth and the nose and throat should be systematically examined for collateral foci of pyogenic infection, and dermatological consultation sought for seemingly trivial lesions on the fingers, face and legs, for scars and pustular lesions on the trunk, macular pigmentation, etc., to say nothing of the more obvious cutaneous signs of tuberculosis, such as erythema induratum, papulonecrotic tuberculids and folliculitis (present in 3 of our cases).

4. Cases of erythema nodosum, whatever their type, should be subjected to periodic reexamination and observation.

5. In the absence of a demonstrable source of pyogenic infection, and even in its presence, the possibility of tuberculous etiology should be seriously entertained and an antituberculosis hygiene considered.

6. The results of the application of the foregoing principles and routine to the dermatoses mentioned, while only partial as yet, have shown so high a percentage of demonstrable and suspected tuberculosis, pulmonary and glandular, osseous and cutaneous, as to lead the writer to suspect that the association is more than coincidental and that it can safely be made a basis for diagnostic and therapeutic decisions in a considerable percentage of cases.

7. It seems not improbable that erythema nodosum especially may be a syndrome of tuberculous as well as diphtheroid or streptococcal origin in an as yet unestablished percentage of cases.

8. Erythema induratum would seem to be susceptible of interpretation as, in a sense, a chronic ulcerative phase of tuberculous erythema nodosum, since intermediate types appear in this series.

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ACUTE PULMONARY EMPHYSEMA OBSERVED DURING THE EPIDEMIC OF INFLUENZAL PNEUMONIA AT CAMP HANCOCK, GEORGIA.

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Prior to the epidemic of influenza at Camp Hancock there occurred in one company an outbreak of hemolytic streptococcus infection of peculiar virulence and uniform course. There was reason for thinking that the spread of disease in these cases was by food or milk infection. One man primarily developed this trouble and in a few days six other men were affected simultaneously, all showing